REMARKS

The foregoing amendment amends claims 1, 9, 20, 42, 64 and 66, cancels claims 46 and 65 and adds new claim 70. Pending in the application are claims 1-45, 47-64 and 66-70, of which claims 1, 9, 20, 22, 29, 42, 64, 66, 67 and 76 are independent. Claims 2-8, 22-41, 49-54, 59, 60 and 67-69 are withdrawn from consideration. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Independent claims 1, 9, 20, 42, 64 and 66 are amended to specify that the fluid interface port has a depth equal to a thickness of an associated side wall and a diameter that is significantly larger than the depth so as to minimize a total volume of the fluid interface port. Support for the amendment can be found throughout the application as originally filed, at least, for example on page 16, line 27-page 17, line 9, page 22, lines 4-18, and as shown in Figures 2A and 2B.

The amendment to independent claims 1, 42, 64 and 66 and new independent claim 70, further specify that the meniscus comprising the virtual wall is substantially co-planar with the side wall of the microchannel in which the meniscus is formed, as described on page 18, lines 13-15 of the original specification and as shown in Figures 3B, 4A and 9A-9E.

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

Claim Objections

Regarding the rejection of claim 46 for failing to further limit the parent claims, claim 46 has been canceled, rendering the objection moot.

35 U.S.C. 102 Rejections

Regarding the rejection of claim 65 under 35 U.S.C. 102(b) as being anticipated by Howitz, claim 65 has been canceled, rendering the rejection moot.

35 U.S.C. 103 Rejections

The Examiner rejects claims 1, 42, 46-48, 56, 58, 63, 64 and 66 under 35 U.S.C. 103(a) as being unpatentable over the Howitz reference.

Applicants have amended independent claims 1, 42, 64 and 66 to specify that each fluid interface port has a depth that is substantially less than the diameter of the fluid interface port to minimize overall volume. The recited fluid interface ports thus have has a disk shape, as shown in Figures 2A and 2B, and described on page 17, lines 19-20, to facilitate *direct* access to the microchannel interior, a feature not taught or suggested in the cited references.

In contrast to the claimed configuration, the microcapillaries of Howitz, which the Examiner considers to be a fluid interface port, comprises a channel having a depth that is significantly *larger* than the cross-section of the channel, which prevents direct interfacing of the channel interior with the ambient.

In addition, claims 1, 42, 64 and 66 further distinguish over the cited references, because the references fail to disclose a fluid interface port forming a virtual wall having a meniscus surface that is co-planar with a side wall in which it is formed. Even if a meniscus were formed in the channel of Howitz, such a meniscus would only be formed in a top portion of the channel and would not align with the side wall in which the channel is formed, as recited in independent claims 1, 42, 64 and 66.

Therefore, claim 1, 42, 46-48, 56, 58, 63, 64 and 66 distinguish patentably over the cited Howitz reference.

The Examiner rejects claims 9-15, 20 and 21 under 35 U.S.C. 103(a) as being unpatentable over the Columbus '313 reference in view of the Bjornson reference. As recognized by the Examiner, the Columbus '313 reference does not disclose a fluid interface port having a dead volume of less than a picoliter or a fluid interface port having a diameter substantially equal to the diameter of a hollow interior. However, the Bjornson reference does not compensate for the deficiencies of the Columbus '313 reference. The cited references, alone or in combination, do not disclose a disk-shaped fluid interface port having a diameter substantially larger than a depth, as now recited in independent claims 9 and 20.

Applicants have amended independent claims 9 and 20 to specify that each fluid interface port has a depth that is substantially less than the diameter of the fluid interface port to minimize overall volume, which distinguishes patentably over the Columbus '313 reference and the Bjornson reference, which have ports in which the diameter is equal to or less than the depth, resulting in an indirect access to the channel interior. The recited fluid interface ports thus have has a disk shape, as shown in Figures 2A and 2B, and described on page 17, lines 19-20, to facilitate *direct* access to the channel interior, a feature not taught or suggested in the cited references.

The Columbus '313 reference is directed to a device for analyzing fluid, including a flow control bridge 36 for providing means for directing liquid flow from drops to ion-selective electrodes 14, 14'. The drops are introduced through liquid ingress apertures 27 to a zone 41. The apertures have a relatively <u>long</u> length and size, resulting in a dead volume that is significantly larger than one picoliter. For example, on page 9, lines 6-8, the Columbus '313 reference indicates that it is preferable for a liquid ingress aperture 27b in a flow control bridge to have a diameter of about <u>0.25 centimeters</u>, which would result in a relatively large dead volume. In addition, the apertures 27 have a depth that is substantially *larger* than a diameter, resulting in a channel shape, in contrast to the claimed fluid interface ports, which have a disk shape.

In addition, the 0.25 centimeter diameter of the liquid ingress apertures of the Columbus '313 reference is significantly larger than the range of between about 25 μm and about 100 μm specified in claim 20. According to the Examiner, the Columbus '313 reference discloses dimensions as low as 60 microns. However, the 60 micron dimension refers to a spacing between two surfaces, <u>not</u> a diameter of an aperture 27, which is significantly larger.

Moreover, the Columbus '313 reference lacks a teaching or suggestion of a plurality of filling apertures having diameters substantially equal to the diameter of an associated microchannel.

The Bjornson reference does not compensate for the deficiencies of the Columbus '313 reference. The Bjornson reference is directed to an apparatus and method for transferring liquids from a well 56 to a sample receiving reservoir 142 via an aperture 630. The aperture 630 of

Bjornson does not have a diameter that is substantially larger than a depth to create a disk-shaped aperture, as recited in independent claims 9 and 20.

In addition, droplets are not directed to the aperture 630 of Bjornson in order to enter a microchannel interior, as recited in independent claims 9 and 20. Rather, liquid in the reservoir 56 is forced *out* via the aperture 630 and into reservoir 142, in contrast to the claimed invention.

In addition, the Bjornson reference does not disclose a fluid interface port in a side wall of a microchannel. Rather, the aperture 630 is formed in a reservoir 56. There is no suggestion that the structure described in Bjornson would be suitable in a microchannel.

Therefore the combination of the Columbus '313 reference and the Bjornson reference fails to make claims 9-15, 20 and 21 obvious.

The Examiner also rejects claims 9, 10, 14, 15, 42 and 55 under 35 U.S.C. 103(a) as being unpatentable over the Columbus '451 reference in view of the Bjornson reference. The Columbus '451 reference also fails to disclose a disk-shaped fluid interface port having a diameter substantially larger than a depth.

The Columbus '451 reference is directed to multi-zone reaction vessel and a method for controlling flow from one zone to another. The reaction vessel 20 of Columbus '451 includes a liquid inlet aperture 46 for permitting the introduction of liquid into zone 22 of the reaction vessel 20. The liquid inlet aperture 46 has a depth that is larger than the diameter, in contrast to the claimed invention. In addition, as specifically set forth in column 5, lines 29-34, the liquid inlet aperture 46 has a diameter of between about 1.0 mm and about 5.0 mm, which would result in a dead volume many times *larger* than one picoliter, and is incapable of forming a virtual wall.

The Bjornson reference does not compensate for the deficiencies of the Columbus '451 reference, as described above.

Regarding the rejection of claims 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over the Columbus '313 reference in view of the Bjornson reference and the Kopf-Sill reference, and the rejection of claims 16, 18 and 19 under 35 U.S.C. 103(a) as being

unpatentable over the Columbus '313 reference in view of the Bjornson reference and the Swierkowski reference, because independent claim 9, from which claims 16-19 depend, distinguishes patentably over the cited references, claims 16-19 are also therefore patentable.

The Examiner also rejects claims 42, 43, 61 and 62 under 35 U.S.C. 103(a) as being unpatentable over the Sundberg reference in view of the Bjornson reference and the Howitz reference, and claims 44 and 45 in further view of the Swedberg reference. However, none of these references discloses the claimed fluid interface port having a disk-shape with a diameter substantially larger than a depth and/or a meniscus surface that is substantially co-planar with a side wall in which the fluid interface port is formed, as described above.

The Examiner also rejects claims 44, 45 over the Howitz reference in view of the Swedberg reference and claims 57, 61, 62 over the Howitz reference in view of the Sundberg reference. Claims 44, 45, 57, 62 and 62 depend on claim 42, which is patentable over the cited references. As described above, the cited references, in particular the Howitz reference, fail to disclose a step of introducing said droplet through a virtual wall in a fluid interface port having a meniscus surface that is substantially co-planar with the side wall in which the virtual wall is formed, where the fluid interface port has a depth equal to a thickness of the sidewall and a diameter that is significantly larger than the depth so as to minimize a total volume of the fluid interface port.

Furthermore, none of the cited references disclose a fluid interface port capable of forming a virtual wall. The virtual wall forms a direct interface between the microchannel interior and the microchannel <u>exterior</u>, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. Even if the devices in the cited references were capable of forming menisci, the menisci would not form virtual walls.

As used in the present application, a "virtual wall" is <u>not</u> an interconnecting channel or simply an opening to a channel. Rather, a virtual wall refers to a particular type of meniscus formed in an <u>opening</u> of a side wall of a microchannel that is sized and dimensioned so that the meniscus essentially replaces the removed portion of the side wall that defines the fluid interface port. A virtual wall does not refer to any and every type of meniscus (i.e., all menisci are not

virtual walls), but rather a meniscus in an opening that is specifically sized and configured so that the fluid flow through the microchannel is not affected by the fact that a portion of the side wall of the microchannel is absent and that the microchannel is exposed to the environment (see the specification at page 17, lines 10-30). The term "virtual wall" is used to denote that the meniscus formed by a fluid in the fluid interface port essentially replaces the removed portion of the side wall that forms the port. The word 'virtual' in the present claims refers to the effect that the overall liquid flow through the separation channel of the electrophoretic system is not influenced by the virtual wall, i.e. the flow of liquid in the micro-plate having a virtual wall is substantially identical to the flow of liquid through an identical micro-plate in which no virtual wall is formed.

The virtual wall forms a direct interface between the microchannel interior and the microchannel exterior, allowing direct access to the liquid in microchannel without introducing dead or unswept volume in the microchannel. In contrast, the channels in the Howitz reference, the Columbus '313 reference, the Columbus 451 reference, the Bjornson reference, the Swedberg reference and the Sundberg reference do not directly interface a microchannel to the environment surrounding the device. These channels also do not form a direct interface, but rather a long, indirect opening with a large dead volume.

The virtual wall of the claimed invention also serves to seal liquid inside of the microchannel through a range of pressures in the microchannel. There is no teaching or suggestion that liquid is sealed in the devices of the cited references.

As set forth in independent claims 1, 9, 42, 64 and 66, a virtual wall also has a relatively low dead volume, i.e., less than about one picoliter. As set forth in the specification, "dead volume" refers to the volume of liquid retained in a fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of the first liquid through the microchannel). The relatively small dead volume provided by the virtual wall results in a direct fluid interface allowing direct injection of a precise volume of sample into the interior of the microchannel from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel,

allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a second substance to be directly injected into the system immediately after a first substance without requiring flushing of the fluid interface port. In contrast, the channels in the Howitz reference, the Columbus '313 reference, the Columbus 451 reference, the Bjornson reference, the Swedberg reference and the Sundberg reference have large dead volumes.

The larger dead volumes in the cited references may lead to dispersion of the sample, a time delay between the time of injection and the time when the sample enters the microchannel, injection inefficiency, potential cross-contamination between different samples and difficulty controlling the amount of sample that actually reaches the microchannel. These problems are avoided or reduced by the use of the fluid interface port forming a virtual wall having a dead volume of less than about one picoliter according to the illustrative embodiment.

<u>New claims</u>

New independent claim 70 is directed to a method of injecting a liquid volume into a microchannel, and also recites that the meniscus of the virtual wall through which the droplet is directed has a meniscus surface that is co-planar with a corresponding side wall, and therefore also distinguishes over the cited references.

In addition, the cited references fail to disclose a fluid interface port defining a meniscus that is co-planar with a side wall in which the port is formed, placing claims 1-8, 42-44, 46-64 and 66-70 are in condition for allowance.

Claims 1-45, 46-64 and 66-70 should also be allowed, because the cited references do not disclose a fluid interface port forming a virtual wall and having a diameter that is significantly larger than a depth of the fluid interface port so as to minimize a total volume.

For at least the foregoing reasons, claims 1-45, 46-64 and 66-70 are patentable over the cited references and in condition for allowance.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 227-7400.

If any additional fee is due with this statement, please charge our Deposit Account No. 12-0080, under Order No. TGZ-001BRCE, from which the undersigned is authorized to draw.

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Respectfully submitted,

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